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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/780,762	02/09/2001	James R. Connor	P04864US2	6610

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EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 04/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/780,762	CONNOR ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-9,12-15,26 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-9,12-15,26 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Acknowledgement is made for the request to establish continued prosecution application (RCE) filed on March 25, 2004. The request for RCE is accepted and is established with the status of the application as follows:

a. the filling date of this RCE is established as 2/09/2001;

b. Claims 1, 12, and 26-27 are amended. Claims 1, 3-9, 12-15, and 26-27 are pending. Claims 2, 10-11, 16-25, 28-31 are cancelled.

2. Applicants' response to the earlier office action filed along with RCE is considered and has been entered.

Response to Arguments

3. Applicants' response to the office action is fully considered and found persuasive.

4. With reference to the rejections made in the previous office action under 103(a), Applicants' arguments and the amendment are fully considered and the rejections are withdrawn herein in view of amendment and new grounds of rejections.

New Grounds of Rejections

5. The instant specification is objected to because of the following informalities:

(i) in Claim 26, "specific primers" is misspelled as "specific promoters". Correction is required.

(i) Claims 14, 15, 26 and 27 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 8, 9.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

(i) Claims 8 and 14 recite the limitation "said primer" in claim 1. There is insufficient antecedent basis for this limitation in the claim. The claim 1 upon which the claims 8 and 14 are dependent, recite two specific primers (plurality). The instant claims lack antecedent basis because the claims recite ***a*** primer (single).

(ii) Claim 5 recites the limitation "said PCR" in claim 1. There is insufficient antecedent basis for this limitation in the claim. The claim 1 upon which the claim 5 is dependent does not recite PCR. Thus instant claim lacks antecedent basis.

(ii) Claims 8 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claims recite said primer is a degenerate primer. The claim 1 upon which the instant claims are dependent recite specific primers (plurality). Thus it is indefinite and unclear because, it is not clear whether the specific primers are degenerate primers or one of the specific primers is a degenerate primer.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-4, 6-7, 9, 12-13, 15, 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Wolfgang et al. (Nucleic Acids Res., Vol. 24, No. 9, pages 1789-1791, 1996).

Wolfgang et al. teach a method of claim 1, 12, 27, for amplifying a cDNA, wherein the method comprises (i) obtaining an mRNA (see page 1789, column2, lines 1-6 of paragraph 2). (ii) reverse transcribing mRNA into cDNA with reverse transcriptase without RNase H activity (superscript RT) so as to form a cDNA-mRNA complex (see page 1789, column 2, lines 1-7 of paragraph 4);

(iii) degrading (alkaline degradation) the mRNA from the cDNA-mRNA complex to form a linear cDNA (see page 1789, column 2, lines 8-12);

(iv) ligating the ends of said linear cDNA to form a circular cDNA (ligating the cDNA into a phagemid vector which results in to a circular plasmid vector comprising the cDNA) (see page 1790, column 2, paragraph 1);

(v) introducing first and second sequence-specific primers to said circular cDNA, wherein the orientation of the primers is complementary to circular cDNA in 5'-3' direction (primers specific for the flanking regions of the ligated cDNA) and Taq DNA polymerase (see page 1790, column 2, paragraph 3, page 1791, column 1, lines 1-5);

(vi) initiating a primer extension amplification (PCR) to increase copy number of said circular cDNA (see page 1790, column 2, paragraph 3, page 1791, column 1, lines 1-5).

With regard to claim 3, Wolfgang et al. disclose that said primer extension is a polymerase chain reaction (see page 1790, column 2, paragraph 3, page 1791, column 1, lines 1-5);

With regard to claim 4, Wolfgang et al. teach that said PCR reaction is employed with Taq DNA polymerase (see page 1790, column 2, paragraph 3, page 1791, column 1, lines 1-5);

With regard to claim 6, Wolfgang et al. disclose harvesting said amplified cDNA (see page 1791, column 1, paragraphs 1-2);

With regard to claims 7 and 13, Wolfgang et al. disclose said ligase is a T4 DNA ligase (see page 1791, column 2, lines 1-3 of paragraph 1);

With regard to claims 9 and 15, 27, Wolfgang et al. disclose said first and second primers are designed to hybridize to from about 4 to about 35 contiguous bases on the said circular cDNA (see the primer sequences for first and second primers used in PCR reaction which comprise sequences specific for the said circular cDNA) (see page 1790, column 2, paragraph 3, page 1791, column 1, lines 1-5);

Thus the disclosure of Wolfgang et al. meets the limitations in the instant claims.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

A. Claims 5, 8, 14, 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wolfgang et al. (Nucleic Acids Res., Vol. 24, No. 9, pages 1789-1791, 1996) in view of Roux (Biotechniques, Vol. 16, No. 5, pages 812-814, 1994).

Wolfgang et al. teach a method for amplifying a cDNA, wherein the method comprises (i) obtaining an mRNA (see page 1789, column2, lines 1-6 of paragraph 2). (ii) reverse transcribing mRNA into cDNA with reverse transcriptase without RNase H activity (superscript RT) so as to form a cDNA-mRNA complex (see page 1789, column 2, lines 1-7 of paragraph 4);

(iii) degrading (alkaline degradation) the mRNA from the cDNA-mRNA complex to form a linear cDNA (see page 1789, column 2, lines 8-12);

(iv) ligating the ends of said linear cDNA to form a circular cDNA (ligating the cDNA into a phagemid vector which results in to a circular plasmid vector comprising the cDNA) (see page 1790, column 2, paragraph 1);

(v) introducing first and second sequence-specific primers to said circular cDNA, wherein the orientation of the primers is complementary to circular cDNA in 5'-3' direction (primers specific for the flanking regions of the ligated cDNA) and Taq DNA polymerase (see page 1790, column 2, paragraph 3, page 1791, column 1, lines 1-5);

(vi) initiating a primer extension amplification (PCR) to increase copy number of said circular cDNA (see page 1790, column 2, paragraph 3, page 1791, column 1, lines 1-5).

Wolfgang et al. also disclose that said primer extension is a polymerase chain reaction (see page 1790, column 2, paragraph 3, page 1791, column 1, lines 1-5); said PCR reaction is employed with Taq DNA polymerase (see page 1790, column 2, paragraph 3, page 1791, column 1, lines 1-5); harvesting said amplified cDNA (see page 1791, column 1, paragraphs 1-2); said ligase is a T4 DNA ligase (see page 1791, column 2, lines 1-3 of paragraph 1); said first and second primers are designed to hybridize to from about 4 to about 35 contiguous bases on the said circular cDNA (see the primer sequences for first and second primers used in PCR reaction which comprise sequences specific for the said circular cDNA) (see page 1790, column 2, paragraph 3, page 1791, column 1, lines 1-5).

However, Wolfgang et al. did not specifically teach use of touchdown PCR and degenerate primers.

Roux teaches a method for amplifying a target nucleic acid using polymerase chain reaction wherein Roux discloses use of touchdown PCR and degenerate primers to amplify the target nucleic acid (see page 814, column 2, paragraph 1). Roux also discloses that employing a series of cycles (touchdown PCR) in which incrementally lowered annealing temperature favors the preferential priming of the primer-template combination with the highest T_m and favors exponential amplification of desired targets and reduces or eliminates non-specific or unwanted PCR products, where unknown degrees of homology were compensated for by using degenerate primers (see page 812, column 3, paragraph 1, page 814, column 1, lines1-4).

Therefore an ordinary practitioner would have been motivated to combine the method for amplifying a cDNA as taught by Wolfgang et al. with the use of touchdown PCR conditions in the presence of degenerate primers as taught by Roux to achieve in developing a method with an enhanced specificity for amplifying a target nucleic acid because Roux taught the advantage of using touchdown PCR conditions to amplify a target nucleic acids with unknown degrees of homology were compensated for by using degenerate primers (see page 812, column 3, paragraph 1, page 814, column 1, lines1-4). An ordinary practitioner would have been motivated to combine the method for amplification of a cDNA as taught by Wolfgang et al. with the inclusion of touchdown PCR conditions and degenerate primers which would result in improving the specificity of the method for amplifying specific target nucleic acids and also reducing non-specific amplified products.

B. Claims 8, and 14, 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wolfgang et al. (Nucleic Acids Res., Vol. 24, No. 9, pages 1789-1791, 1996) in view of Liang et al. (USPN. 5,599,672).

Wolfgang et al. teach a method for amplifying a cDNA, wherein the method comprises (i) obtaining an mRNA (see page 1789, column2, lines 1-6 of paragraph 2). (ii) reverse transcribing mRNA into cDNA with reverse transcriptase without RNase H activity (superscript RT) so as to form a cDNA-mRNA complex (see page 1789, column 2, lines 1-7 of paragraph 4);

(iii) degrading (alkaline degradation) the mRNA from the cDNA-mRNA complex to form a linear cDNA (see page 1789, column 2, lines 8-12);

(iv) ligating the ends of said linear cDNA to form a circular cDNA (ligating the cDNA into a phagemid vector which results in to a circular plasmid vector comprising the cDNA) (see page 1790, column 2, paragraph 1);

(v) introducing first and second sequence-specific primers to said circular cDNA, wherein the orientation of the primers is complementary to circular cDNA in 5'-3' direction (primers specific for the flanking regions of the ligated cDNA) and Taq DNA polymerase (see page 1790, column 2, paragraph 3, page 1791, column 1, lines 1-5);

(vi) initiating a primer extension amplification (PCR) to increase copy number of said circular cDNA (see page 1790, column 2, paragraph 3, page 1791, column 1, lines 1-5).

Wolfgang et al. also disclose that said primer extension is a polymerase chain reaction (see page 1790, column 2, paragraph 3, page 1791, column 1, lines 1-5); said PCR reaction is employed with Taq DNA polymerase (see page 1790, column 2, paragraph 3, page 1791, column 1, lines 1-5); harvesting said amplified cDNA (see page 1791, column 1, paragraphs 1-2); said ligase is a T4 DNA ligase (see page 1791, column 2, lines 1-3 of paragraph 1); said first and second primers are designed to hybridize to from about 4 to about 35 contiguous bases on the

said circular cDNA (see the primer sequences for first and second primers used in PCR reaction which comprise sequences specific for the said circular cDNA) (see page 1790, column 2, paragraph 3, page 1791, column 1, lines 1-5).

However, Wolfgang et al. did not specifically teach use of degenerate primers.

Liang et al. teach a method for amplifying mRNA using specific primers with degenerate sequences (see column 4, lines 49-67, column 5, lines 1-64). Liang et al. also disclose that the use of different primers with degenerate or alterable primer sequences would aid in identifiying and isolating virtually any or all of the mRNAs from any cell type or any stage of the cell cycle, including very low abundance mRNAs (see column 3, lines 15-24). Further Liang et al. disclose that primers for any consensus sequence can be readily be designed and degeneracy can be incorporated at one or more sites allowing the primer to hybridize to a high percentage, greater than 50% of the mRNAs containing the desired consensus sequence (see column 14, lines 24-29).

Therefore an ordinary practitioner would have been motivated to combine the method for amplifying a cDNA as taught by Wolfgang et al. with the use of degenerate primer sequences as taught by Liang et al. to achieve in developing improved method for amplifying any target nucleic acid including low abundance mRNAs because Liang et al. taught the advantage of using primers for consensus sequences with the incorporation of degeneracy at one or more sites to amplify any or all mRNAs from any type of cell including low-abundance mRNAs with high specificity to hybridize to a high percentage of mRNAs containing desired consensus sequences (see column 3, lines 15-24, column 14, lines 24-29). An ordinary practitioner would have been motivated to combine the method for amplification of a cDNA as taught by Wolfgang et al. with

the inclusion of degenerate primers which would result in amplifying any mRNA target including low-abundance RNAs.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
April 13, 2004

JEHANNE SITTON
PRIMARY EXAMINER
4/13/04